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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/696,070	10/25/2000	James E. Rothman	A31488-I-065360.0141	3515

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EXAMINER

SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
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1652

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DATE MAILED: 05/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary

Application No.

09/696,070

Applicant(s)

ROTHMAN ET AL.

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14,16,18 and 44-55 is/are pending in the application.
- 4a) Of the above claim(s) 16,18,44,45 and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14,46,47,49,50 and 53 is/are rejected.
- 7) ☒ Claim(s) 51,52,54 and 55 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 October 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's response, on February 24, 2003, Paper No. 8, to the first Office Action on the Merits of this case is acknowledged. It is acknowledged that applicants have cancelled Claims 15, 17, and 19, amended Claims 14, 16, and 18, and added Claims 44-55. Claims 14, 16, 18, and 44-55 are pending.

Election/Restrictions

This application contains claims directed to the following patentably distinct species of the claimed invention:

Claims 18, 44, and 46-47 include the following species of oligomerization domain:

Derived from a cartilage matrix protein,

Derived from phospholamban,

SEQ ID NO: 1,

SEQ ID NO: 2,

SEQ ID NO: 7,

Thrombospondin,

TSP3,

TSP4,

SEQ ID NO: 3,

SEQ ID NO: 4,

SEQ ID NO: 5, and

SEQ ID NO: 6.

These species of Claims 18, 44, and 46-47 are patentably distinct because they are

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physically and functionally distinct chemical entities.

Claim 49 includes the following species of sequences at the carboxy terminus of the KDELr inhibitor: X-Asp-Glu-Leu where X is:

Lys,

His, and

Asp.

These species of Claim 49 are patentably distinct because they are physically and functionally distinct chemical entities.

Claims 51 and 52 include the following species of polynucleotides encoding KDELr inhibitor protein:

SEQ ID NO: 14 or encoding the protein set forth by SEQ ID NO: 13,

SEQ ID NO: 16 or the protein encoded by SEQ ID NO: 15,

SEQ ID NO: 18 or encoding the protein set forth by SEQ ID NO: 17,

SEQ ID NO: 20 or encoding the protein set forth by SEQ ID NO: 19,

SEQ ID NO: 22 or encoding the protein set forth by SEQ ID NO: 21,

SEQ ID NO: 24 or encoding the protein set forth by SEQ ID NO: 23,

SEQ ID NO: 26 or encoding the protein set forth by SEQ ID NO: 25,

SEQ ID NO: 28 or encoding the protein set forth by SEQ ID NO: 27,

SEQ ID NO: 30 or encoding the protein set forth by SEQ ID NO: 29, and

SEQ ID NO: 35 or encoding the protein set forth by SEQ ID NO: 34.

These species of Claims 51 and 52 are patentably distinct because they are physically and functionally distinct chemical entities.

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Applicant is required under 35 U.S.C. 121 to elect a single disclosed species of oligomerization domain, carboxy terminus of the KDELr inhibitor, and KDELr inhibitor protein for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 14, 16, and 45 are generic.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

During a telephone conversation with Joe Cappola on May 7, 2003 a provisional election was made without traverse to prosecute the species TSP3 of Claims 18 and 44-48, the species Lys of Claim 49, and the species SEQ ID NO: 27 and 28 of Claims 51, 52, 54, and 55. Affirmation of this election must be made by applicant in replying to this Office action.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Claims 16, 18, 44, 45, and 48 are not deemed to be encompassed by the elected invention and/or elected species. Therefore, said claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim. Claims 14 is hereby reconsidered and Claims 47 and 49-55 are considered.

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Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is noted that copending Application SN# 09/800,445 has the same inventors and title as the present application suggesting that, the claims of 09/800,445 and this application may recite the same or overlapping Inventions. Since 09/800,445 is not presently available for review, no determination has been made as to whether or not a double patenting rejection over the claims from 09/800,445 should be applied to the claims of the instant application. If, upon availability of the above application to the Examiner, it is determined that there are conflicting claims between 09/800,445 and the instant application, double patenting will not be considered as new ground(s) of rejection.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

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the invention. The recitation in Claim 47 of "...where the thrombospondin protein is TSP3" wherein Claim 47 depends from Claim 46 which recites "... where the trimerization domain is derived from a thrombospondin protein" is indefinite. Thrombospondin 3 comprises a pentamerization domain (Qabar et al, 1995), not a trimerization domain. Therefore, Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. For purposes of examination it is assumed that Claim 47 is meant to recite "...wherein the thrombospondin pentamerization domain is TSP3" and should depend from Claim 16.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 14, 49, 50, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al, 1993 (in IDS) in view of Benaroudj et al, 1995 and further in view of Ausubel, 1997 and Bandman et al, 1998. Wilson et al teach that a peptide, comprising the sequence X-Asp-Glu-Leu wherein X is a Lys, inhibits binding of a radiolabelled C-terminal fragment of the heat shock protein BiP, [¹²⁵I]-YTSEKDEL, to the KDELr (Figs 1 and 4). Wilson et al do not teach their KDELr inhibitor comprising an oligomerization domain. However, Benaroudj et al teaches that heat shock proteins, which bind to KDELrs, oligomerize (Figs 3 and Table 1) suggesting that a KDELr inhibitor would be more effective if oligomerized. The identity of many oligomerization domains was well known in the art, as described by Applicants in Paper No. 8, page 10, para 3 to page 12, para 1. It would have also been obvious to a person of

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ordinary skill in the art that oligomerization of the KDELr inhibitor of Wilson et al would provide the advantage of cooperative binding of the inhibitor and, thus, increase the efficiency of KDELr inhibition. It would have also been obvious to a person of ordinary skill in the art to put a linker between the KDEL motif and the oligomerization domain. Furthermore, it would have been obvious to a person of ordinary skill in the art to prepare a polynucleotide to produce a protein inhibitor, comprising the peptides of Wilson et al and an oligomerization domain, in host cells (Ausubel et al). The production and use of polypeptides comprising the peptides of Wilson et al and an oligomerization is suggested by Bandman et al wherein they state that, antagonist that bind specifically to the KDELr can be used as therapeutics (Abstract). Motivation to make and use polynucleotides encoding polypeptides comprising the peptides of Wilson et al and an oligomerization domain in the treatment plan of Bandman et al is high because, the peptides of Wilson et al are specific antagonists of the KDELr and, as such, are predicted to be useful as therapeutics (Bandman et al). The expectation of success is high as preparation of polynucleotides for recombinant production of encoded proteins is common in the art.

Therefore, Claim 14, 49, 50, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al, 1993 (in IDS) in view of Benaroudj et al, 1995 and further in view of Ausubel, 1997 and Bandman et al, 1998.

Claims 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al, 1993 (in IDS) in view of Benaroudj et al, 1995, Ausubel, 1997, and Bandman et al, 1998 and further in view of Qabar et al, 1995. The teachings of Wilson et al, Benaroudj et al, Ausubel, and Bandman et al, are described above. Neither Wilson et al, Benaroudj et al, Ausubel, nor Bandman et al teach the use of the oligomerization domain of TSP3. However,

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Qabar et al teach that TSP3 is oligomerized via pentamerization domains linked by two disulfide bridges (Figs 3 and 4). It would have been obvious to a person of ordinary skill in the art to use the pentamerization domain of TSP3 to prepare a polynucleotide encoding a KDELr inhibitor comprising said domain and the peptides of Wilson et al. The preparation of a polynucleotide encoding a KDELr inhibitor comprising the pentamerization domain of thrombospondin 3 is motivated by the advantageous stabilization of the oligomerized inhibitor by the disulfide linkages present in said pentamerization domain (Qabar et al; Fig 5). The expectation of success is high as, preparation of polynucleotides for recombinant production of encoded proteins is common in the art. Therefore, Claim 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al, 1993 (in IDS) in view of Benaroudj et al, 1995, Ausubel, 1997, and Bandman et al, 1998 and further in view of Qabar et al, 1995.

Allowable Subject Matter

Claims 51, 52, 54, and 55 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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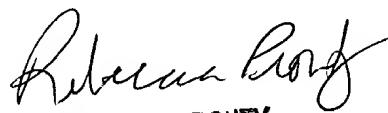
will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.


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PRIMARY EXAMINER
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